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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/683,656	10/09/2003	Sundeep Dugar	219002029600	2874
25225 7590 02/09/2007 MORRISON & FOERSTER LLP 12531 HIGH BLUFF DRIVE SUITE 100 SAN DIEGO, CA 92130-2040			EXAMINER CHANG, CELIA C	
			ART UNIT	PAPER NUMBER
			1625	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/09/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/683,656	<b>Applicant(s)</b> DUGAR, SUNDEEP	
	<b>Examiner</b> Celia Chang	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 22 November 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1-30 and 32-39 is/are pending in the application.
- 4a) Of the above claim(s) 11 and 34-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-3, 12, 15, 19, 23, 26 and 27 is/are rejected.
- 7) ☐ Claim(s) 4-10, 13-14, 16-18, 20-22, 24-25, 28-30, 32-33, 39 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Applicant's election of Group II with species of example 20 of p.41 in the reply filed on Nov. 20, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants were advised in the restriction requirement that :

"Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention."

Applicants in traversing the restriction provided no factual evidence or presented arguments the species are obvious variants of each other. In the instant case, it was evidenced that when "l+k" is 1, the compounds have VEGF receptor inhibition activity (CA 2007:17769); when "l+k" is 2, Z<sup>1</sup> is CR<sup>5</sup>, the compounds have antihistamine activity (CA 104:68856); when "l+k" is 3, the compounds have protein kinase inhibiting activity (CA 146:27814). The divergent subject matter covering structurally diverse ring system do no share common core for any known utility. The search for each independent and distinct core system must be conducted separate and the search for all the non-extensive core compounds is a tremendous burden for the office.

Claims 31, 40-41 have been canceled.

Based on the species election, the subject matter being examiner is the combination of claims 7 and 10 wherein l=1, k=1, Z<sup>1</sup> is N. Claims 1-10, 12-30, 32-33, 39 reading on formula I wherein l=1, k=1, Z<sup>1</sup> is N is examined.

Claims 11, 34-38 and the *remaining* subject matter of claims 1-10, 12-30, 32-33 and 39 are withdrawn from consideration per 37 CFR 1.142(b).

Art Unit: 1625

2. Claims 1-3, 12, 15, 19, 23, 26-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims contain such ambiguous and indefinite terms which provided very confusing structural arrangements of the claims thus rendered the scope of the claims indefinite.

It is unclear what is the chemical structure of 'non-interfering substituent'. On page 4, the noninterfering substituent is described to be a substituent which leaves the ability of the compound of formula (1) to inhibit p38 activity qualitatively intact. One must first find a compound which is encompassed by formula 1 that has p38 inhibiting activity, then find a substituent which upon derivatization of the parent compound would not affect only the quality not the quantity of the inhibiting activity. The activity of course is determined by physiological assays (see p.4). Such description provided no structural delineation of the "compounds". The scope of the compound claims thus cannot be ascertained.

It is unclear what is the chemical structure of "COR<sup>2</sup> or an isostere thereof". On page 11, a few structural surrogate of the carboxylic acid functional group was disclosed. It is unclear what is the supposed replacement isostere is. Please note that medicinal chemistry is well developed in the chemical isosteric replacement of functional groups (see King or Patani). An carboxylic acid surrogate, is independent and distinct from a carbonyl surrogate or an aldehyde surrogate. Without a definitive chemical structure, it is indefinite as to what is being isosterically replaced, thus, the scope of the claims cannot be ascertained.

It is unclear as to what is "alkyl, alkenyl.....or the heteroatom containing forms thereof". Or "two R (or R<sup>4</sup>)... may form a ring or fused ring and their heteroforms thereof". Initially, it is pointed out that if the two R<sup>4</sup> forms a fused ring is referring to a fused ring piperazine, it is *no within the scope of election*, thus should be restricted out. It is unclear of how these moieties having heteroatoms can be linked to form what ring or what heteroforms thereof. Not only the scope of the claims cannot be ascertained, the scope of claim 19 finds no antecedent basis in the base claim since no subject matter of two R<sup>4</sup> can be joined to form ring was described in claim 1. Although applicants can be his or her lexicographer, the claims are drawn to chemical compounds, thus, terms must clearly delineate chemical structure.

Art Unit: 1625

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by

Houpis CA 122:105718, see RN 160729-91-9;

Furuya et al. CA 124:202226, see RN 174070-51-0, 174070-83-8, 174070-84-9,  
(please not oxo-substituted fully aromatized ring is tautomeric to hydroxyl substitution);

Kim et al. CA 125:58548, see RN 177792-85-7;

Suzuki et al. CA 127:135807, see RN 174070-83-8, 192885-85-1;

Ewing et al. CA 131:130007, see RN 234102-19-3.

The structural delineated compounds of the prior art anticipated the instant claims when R1 is H or noninterfering substituents, L1 and L2 are linker and all other optionally substitutions are noninterfering substituents.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

Art Unit: 1625

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzzetti et al.

CA 124:260834 supplemented by King in view of Bundgaard.

Determination of the scope and content of the prior art (MPEP §2141.01)

Buzzetti et al. disclosed tyrosine kinase inhibitors for which a species of isosteric carbonyl compound (see King table 2) is delineated as RN 175075-88-4.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art compounds is that instead of a free piperazine, the instant claims requires an L2A substituent. The L2A structure broadly disclosed can be benzoyl. N-acylated modification of an amine drug is conventionally known as the prodrug formulation (Bundgaard p.27-28).

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art in possession of the above references would be motivated to modify the known drug of Buzzetti et al. with the prodrug acylation because the skilled artisan would expect the inactive prodrug would be converted to the tyrosine kinase inhibitor in vivo and such modification would overcome solubility problems in formulation (see Bundgaard p.1).

5. Applicants' attention is drawn to CA 143:347150 or CA 143:133351 for which two US pregrant publications US 20050209269 and US 20050256151 were available. Please note that the compounds encompassed by the pregrant claims are fully encompassed by the instant claims, especially claim 1 wherein the scope requires no limitation for linker or noninterfering substituents for all the moieties. The two copending applications would be 102(f) or (g) references since none of the compounds disclosed in CA 143:347150 or CA 143:133351 was disclosed by the instant application, yet are included in the claims. The issue of who is the first to invent such concept must be resolved.

6. Claims 4-10, 13-14, 16-18, 20-22, 24-25, 28-30, 32-33, 39 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

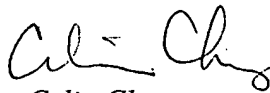
Art Unit: 1625

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie, Ph. D., can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang  
Feb. 1, 2007

  
Celia Chang  
Primary Examiner  
Art Unit 1625